

10/728,339

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USPATFULL/USPAT2
NEWS 9 MAY 30 The F-Term thesaurus is now available in CA/CAPLUS
NEWS 10 JUN 02 The first reclassification of IPC codes now complete in
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NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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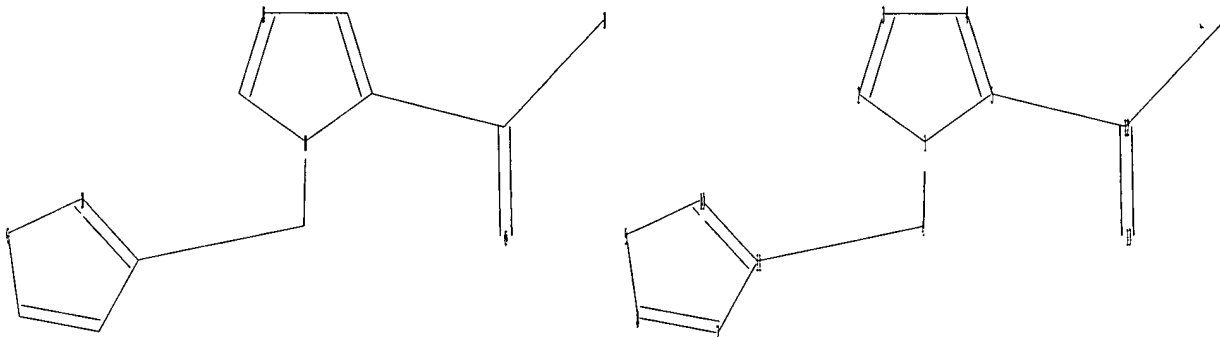
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=>

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chain nodes :
6 12 13 14
ring nodes :
1 2 3 4 5 7 8 9 10 11
chain bonds :
1-6 5-12 6-11 12-13 12-14
ring bonds :
1-2 1-5 2-3 3-4 4-5 7-8 7-11 8-9 9-10 10-11
exact/norm bonds :
1-2 1-5 1-6 2-3 3-4 10-11 12-13 12-14
exact bonds :
4-5 5-12 6-11 7-8 7-11 8-9 9-10
isolated ring systems :
containing 1 : 7 :

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Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 14:48:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3 TO ITERATE

100.0% PROCESSED 3 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 3 TO 163
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 ful

FULL SEARCH INITIATED 14:48:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 74 TO ITERATE

100.0% PROCESSED 74 ITERATIONS 23 ANSWERS
SEARCH TIME: 00.00.01

L3 23 SEA SSS FUL L1

=> file caplus

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FILE 'CAPLUS' ENTERED AT 14:48:33 ON 09 AUG 2006
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=> s 13

L4 2 L3

=> d 14 ibib hitstr abs 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1011962 CAPLUS

DOCUMENT NUMBER: 142:6532

TITLE: Preparation of imidazolecarboxamides as factor Xa and/or factor VIIa inhibitors

INVENTOR(S): Nazare, Marc; Bauer, Armin; Wehner, Volkmar; Will, David William; Matter, Hans; Wagner, Michael; Schreuder, Herman

PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany

SOURCE: Eur. Pat. Appl., 90 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1479674	A1	20041124	EP 2003-11307	20030519
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CA 2507624	AA	20040617	CA 2003-2507624	20031120
WO 2004050636	A2	20040617	WO 2003-EP12996	20031120
WO 2004050636	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1569927	A2	20050907	EP 2003-778324	20031120
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BR 2003017003	A	20051025	BR 2003-17003	20031120
JP 2006514093	T2	20060427	JP 2004-570676	20031120
US 2004171604	A1	20040902	US 2003-728339	20031204
PRIORITY APPLN. INFO.:			EP 2002-27120	A 20021204
			US 2003-463449P	P 20030416
			EP 2003-11307	A 20030519
			US 2003-507338P	P 20030930
			WO 2003-EP12996	W 20031120

OTHER SOURCE(S): MARPAT 142:6532

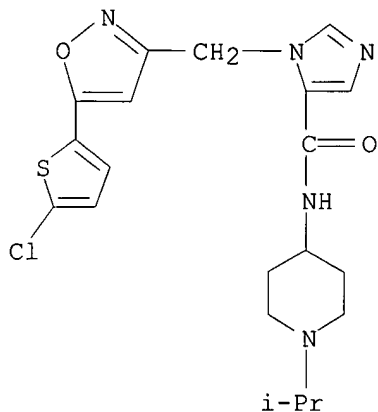
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701292-92-4P 701292-99-1P 701293-13-2P
701293-14-3P 796857-04-0P 796857-06-2P

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(claimed compound; preparation of imidazolecarboxamides as factor Xa and/or
factor VIIa inhibitors)

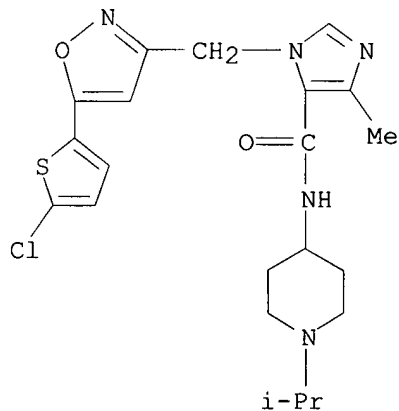
RN 701292-53-7 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-
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NAME)



RN 701292-61-7 CAPLUS

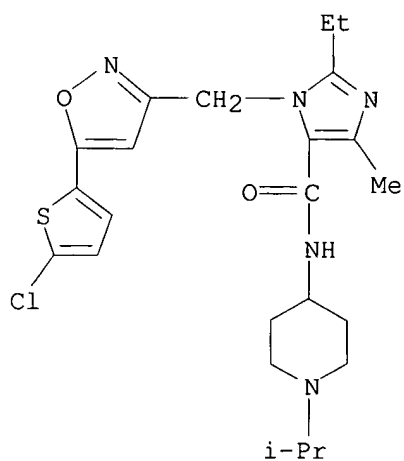
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RN 701292-62-8 CAPLUS

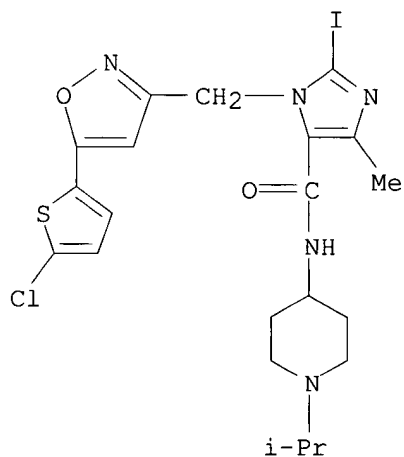
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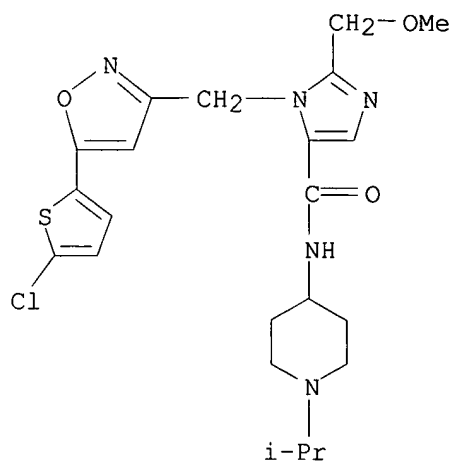
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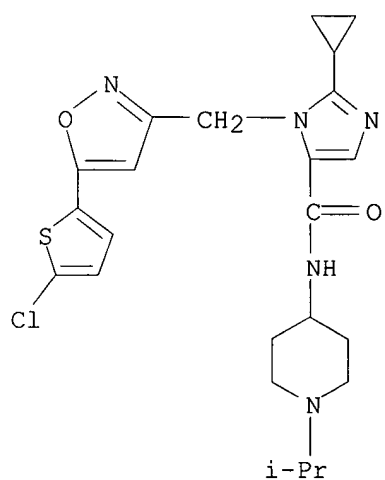
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10/728,339



RN 701292-75-3 CAPLUS

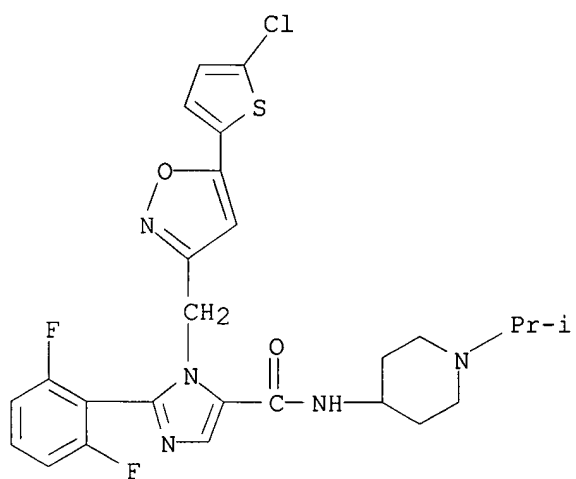
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(9CI) (CA INDEX NAME)



RN 701292-76-4 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-(2,6-difluorophenyl)-N-[1-(1-methylethyl)-4-piperidinyl]-
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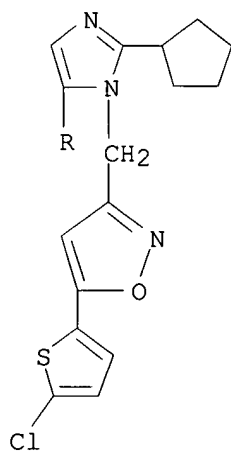
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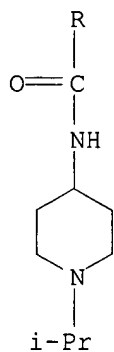


RN 701292-77-5 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-cyclopentyl-N-[1-(1-methylethyl)-4-piperidiny]-
(9CI) (CA INDEX NAME)

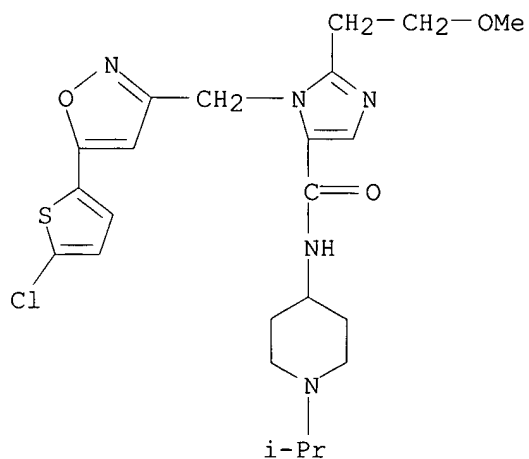
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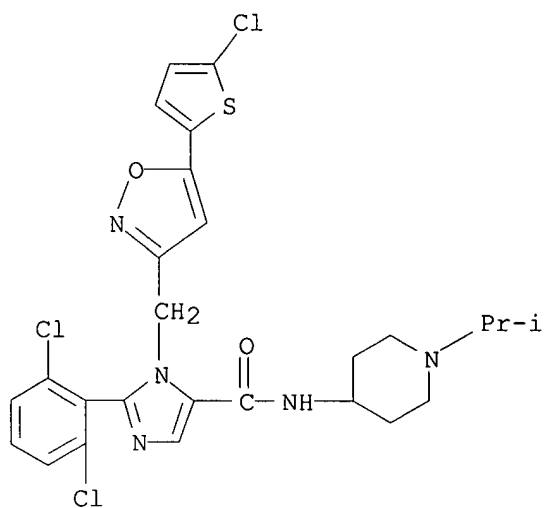
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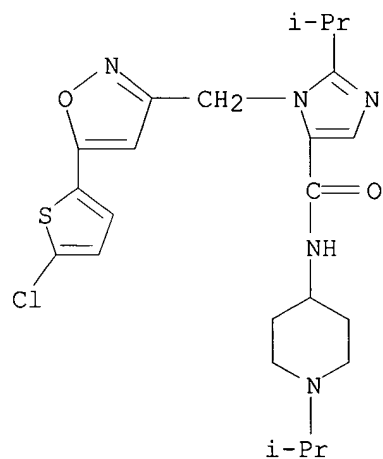
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10/728,339



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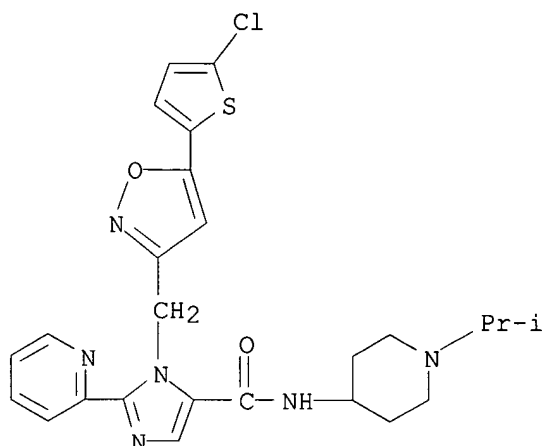
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(9CI) (CA INDEX NAME)



RN 701292-81-1 CAPLUS

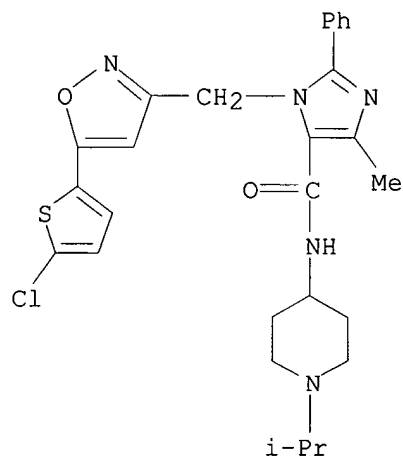
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(9CI) (CA INDEX NAME)

10/728,339



RN 701292-82-2 CAPLUS

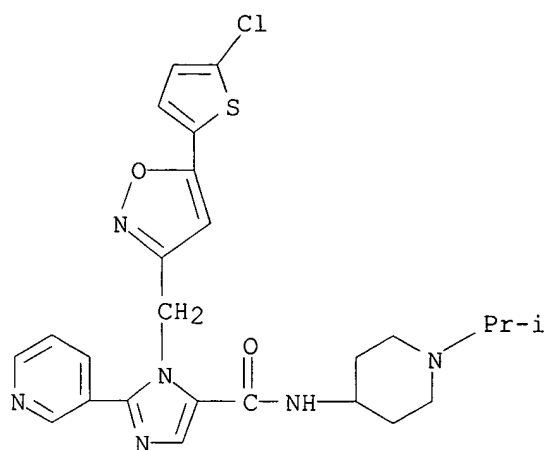
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]-2-phenyl-(9CI) (CA INDEX NAME)



RN 701292-86-6 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidinyl]-2-(3-pyridinyl)-(9CI) (CA INDEX NAME)

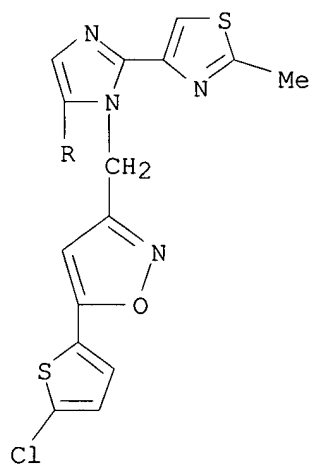
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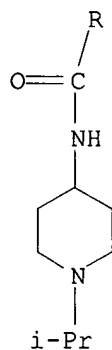


RN 701292-87-7 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidiny]-2-(2-methyl-4-thiazolyl)- (9CI) (CA INDEX NAME)

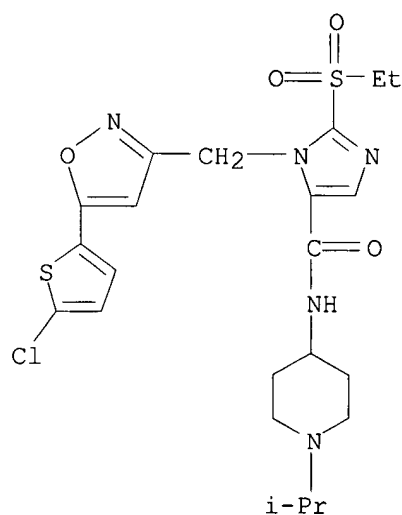
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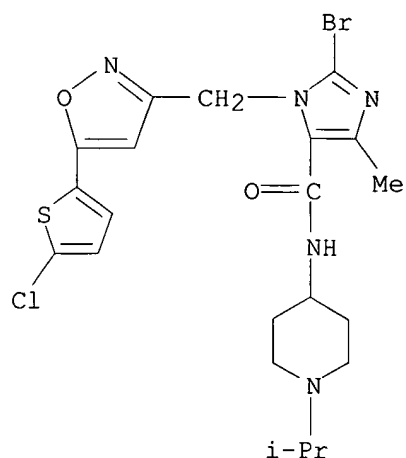
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RN 701292-99-1 CAPLUS

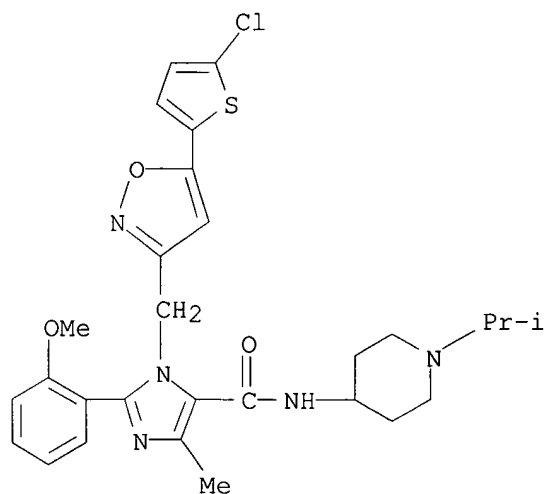
CN 1H-Imidazole-5-carboxamide, 2-bromo-1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]- (9CI)
(CA INDEX NAME)

10/728,339



RN 701293-13-2 CAPLUS

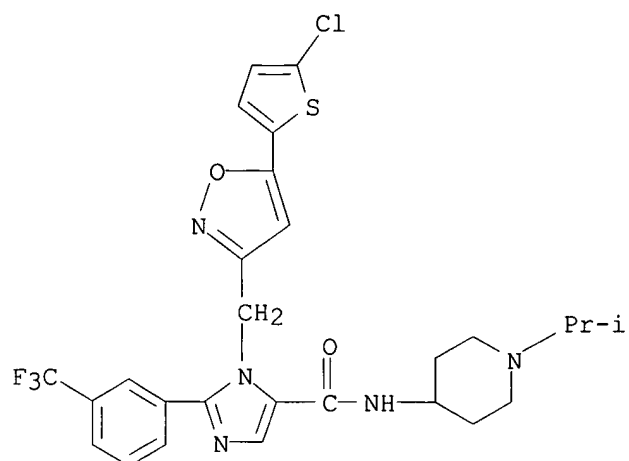
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RN 701293-14-3 CAPLUS

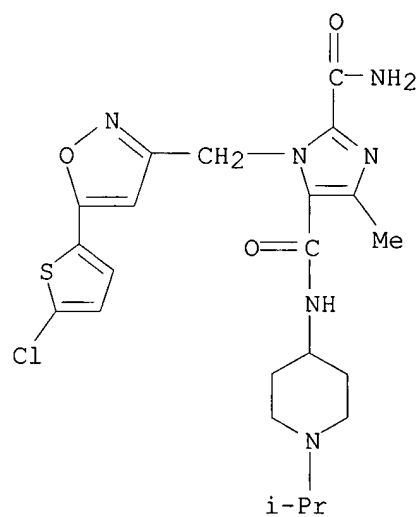
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10/728,339



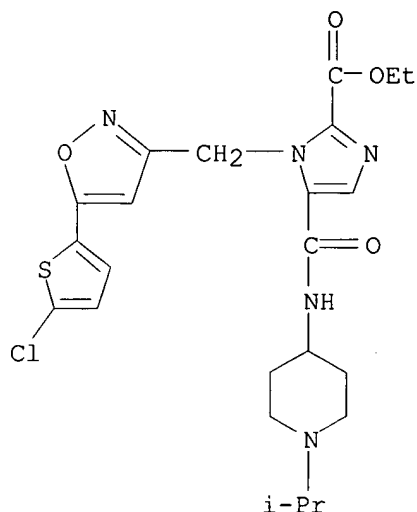
RN 796857-04-0 CAPLUS

CN 1H-Imidazole-2,5-dicarboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-4-methyl-N5-[1-(1-methylethyl)-4-piperidiny]- (9CI)
(CA INDEX NAME)

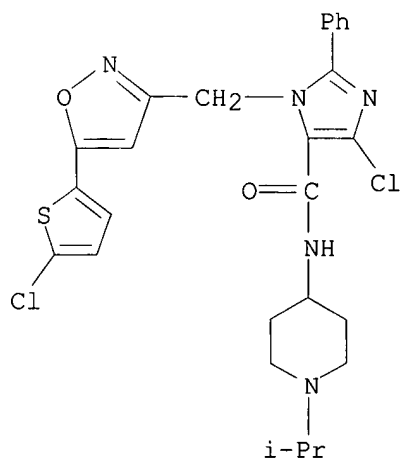


RN 796857-06-2 CAPLUS

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IT 701292-59-3P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of imidazolecarboxamides as factor Xa and/or factor VIIa inhibitors)
 RN 701292-59-3 CAPLUS
 CN 1H-Imidazole-5-carboxamide, 4-chloro-1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidinyl]-2-phenyl- (9CI)
 (CA INDEX NAME)



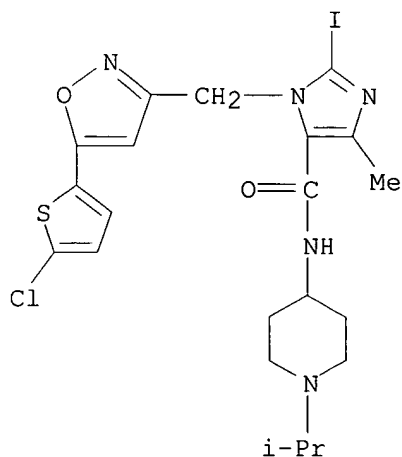
IT 796857-12-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of imidazolecarboxamides as factor Xa and/or factor VIIa inhibitors)
 RN 796857-12-0 CAPLUS
 CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-iodo-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

10/728,339

CM 1

CRN 701292-65-1

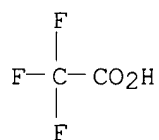
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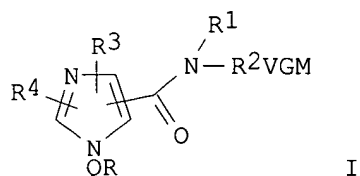
CM 2

CRN 76-05-1

CMF C2 H F3 O2



GI



AB Title compds. [I; R = (substituted) mono- or bicyclic aryl, pyridinyl, pyrimidinyl, indolyl, isoindolyl, indazolyl, phthalazinyl, quinolyl, etc.; Q = bond, aminocarbonylalkyl, aminocarbonylamino, carbonylamino, etc.; R¹ = H, (substituted) alkyl, aryl, heterocyclyl, etc.; R² = bond, alkylene; R¹R³ = atoms to form a (substituted) 6-8 membered ring containing 1-4 N, O, S atoms; R¹NR²V = atoms to form a (substituted) 4-8 membered ring containing 1-4 N, O, S atoms; R³, R⁴ = H, halo, NO₂, cyano, hydroxyaminocarbonyl, methoxyaminocarbonyl, (substituted) alkyl, Ph, aminoalkyl, sulfonylamino, heterocyclalkyl, cycloalkylalkyl, specified azolyl, etc.; G = bond,

(CH₂)_mNR10SO₂NR10(CH₂)_n, etc.; m, n = 0-6; M = H, (substituted) alkyl, aminocarbonyl, aminoalkyl, etc.; R10 = H, alkyl, hydroxyalkyl, alkoxyalkyl, perfluoroalkyl], were prepared. Thus, 3-[5-(5-chlorothiophen-2-yl)isoxazol-3-ylmethyl]-2-iodo-5-methyl-3H-imidazole-4-carboxylic acid (preparation given), N-ethylmorpholine, and TOTU were stirred 30 min. in CH₂Cl₂; 1-isopropylpiperidin-4-ylamine hydrochloride (preparation given) was added followed by stirring for 2 h to give thus, 3-[5-(5-chlorothiophen-2-yl)isoxazol-3-ylmethyl]-2-iodo-5-methyl-3H-imidazole-4-carboxylic acid (1-isopropylpiperidin-4-yl)amide, isolated as the trifluoroacetate. The latter inhibited factor Xa with K_i = 0.001 μM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:470325 CAPLUS

DOCUMENT NUMBER: 141:38613

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PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany

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EP 1426364	A1	20040609	EP 2002-27120	20021204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2507624	AA	20040617	CA 2003-2507624	20031120
WO 2004050636	A2	20040617	WO 2003-EP12996	20031120
WO 2004050636	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
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AU 2003285336	A1	20040623	AU 2003-285336	20031120
EP 1569927	A2	20050907	EP 2003-778324	20031120
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BR 2003017003	A	20051025	BR 2003-17003	20031120
JP 2006514093	T2	20060427	JP 2004-570676	20031120
US 2004171604	A1	20040902	US 2003-728339	20031204
PRIORITY APPLN. INFO.:			EP 2002-27120	A 20021204
			US 2003-463449P	P 20030416
			EP 2003-11307	A 20030519
			US 2003-507338P	P 20030930
			WO 2003-EP12996	W 20031120

OTHER SOURCE(S): MARPAT 141:38613

IT 701292-53-7P 701292-59-3P 701292-61-7P

701292-62-8P 701292-65-1P 701292-69-5P

701292-75-3P 701292-76-4P 701292-77-5P

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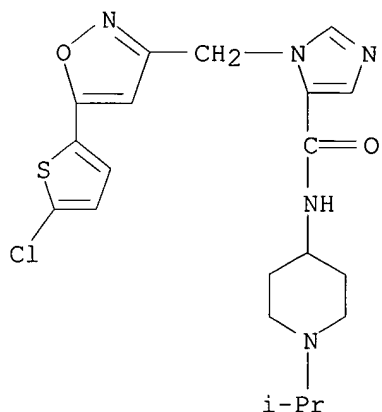
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701293-13-2P 701293-14-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazole derivs. useful as factor Xa inhibitors)

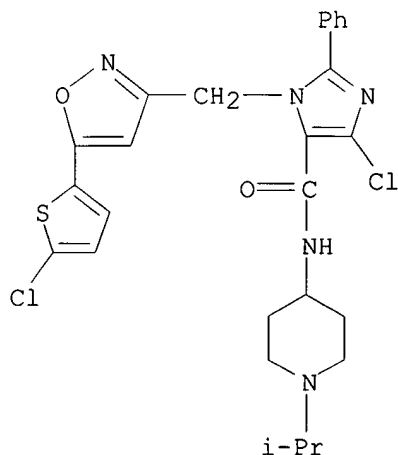
RN 701292-53-7 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 701292-59-3 CAPLUS

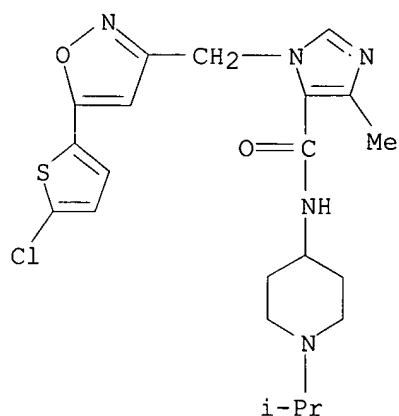
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RN 701292-61-7 CAPLUS

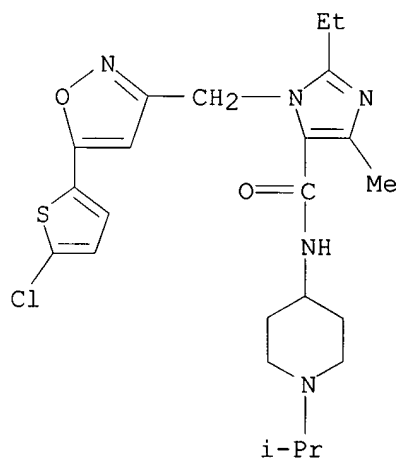
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RN 701292-62-8 CAPLUS

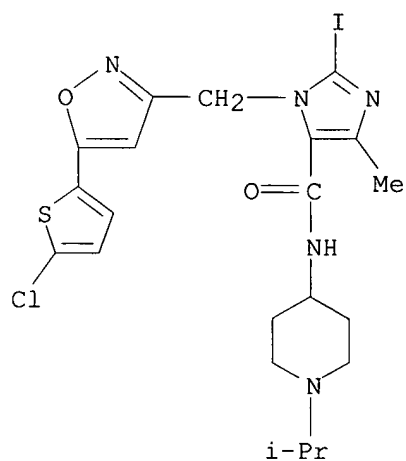
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(9CI) (CA INDEX NAME)



RN 701292-65-1 CAPLUS

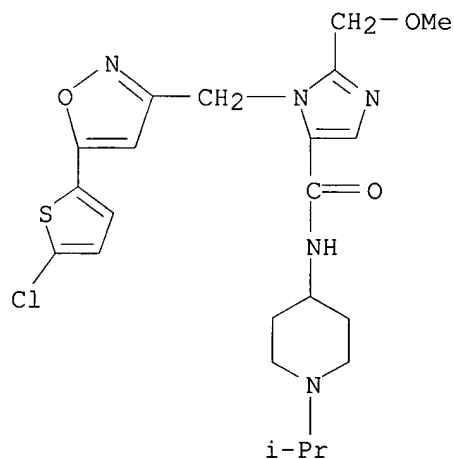
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-iodo-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]-
(9CI) (CA INDEX NAME)

10/728,339



RN 701292-69-5 CAPLUS

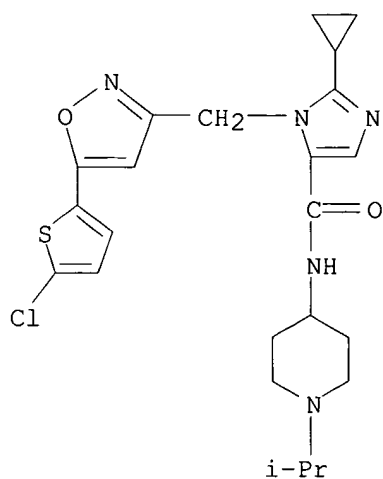
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-(methoxymethyl)-N-[1-(1-methylethyl)-4-piperidinyl]-
(9CI) (CA INDEX NAME)



RN 701292-75-3 CAPLUS

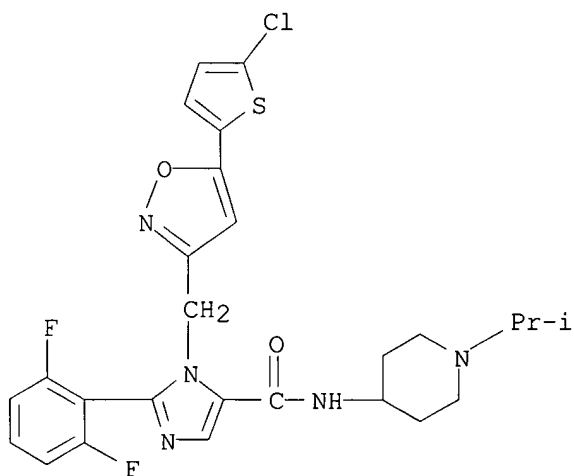
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-cyclopropyl-N-[1-(1-methylethyl)-4-piperidinyl]-
(9CI) (CA INDEX NAME)

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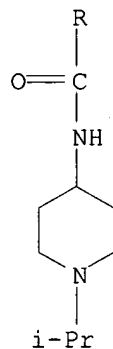
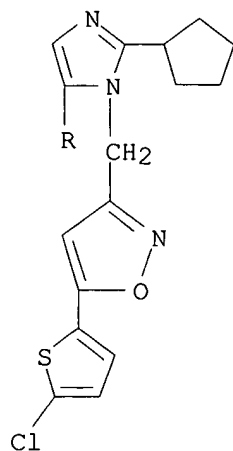
RN 701292-76-4 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-(2,6-difluorophenyl)-N-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



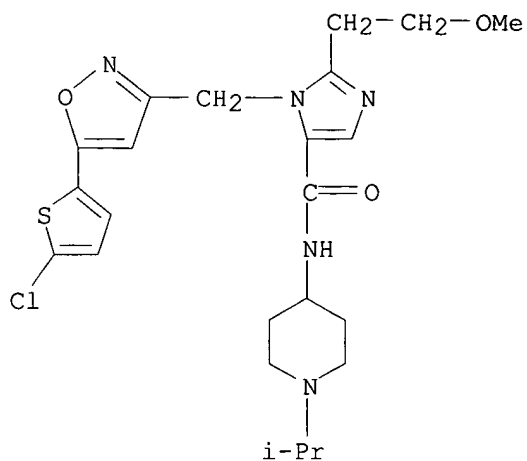
RN 701292-77-5 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-cyclopentyl-N-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



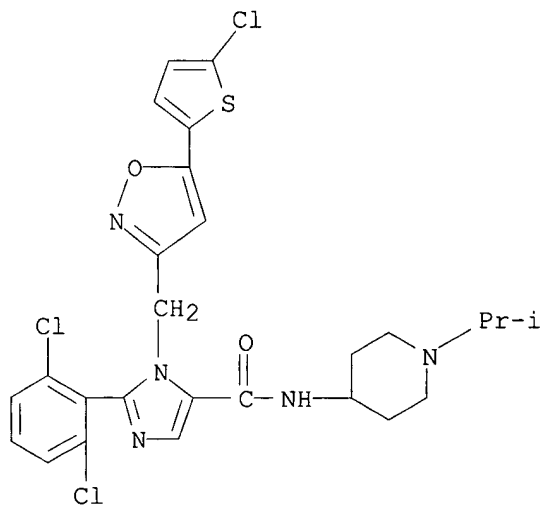
RN 701292-78-6 CAPLUS
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 (9CI) (CA INDEX NAME)

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RN 701292-79-7 CAPLUS

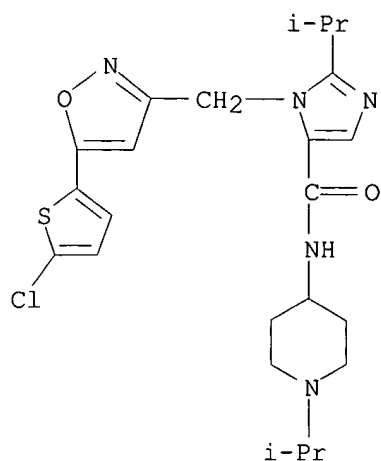
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RN 701292-80-0 CAPLUS

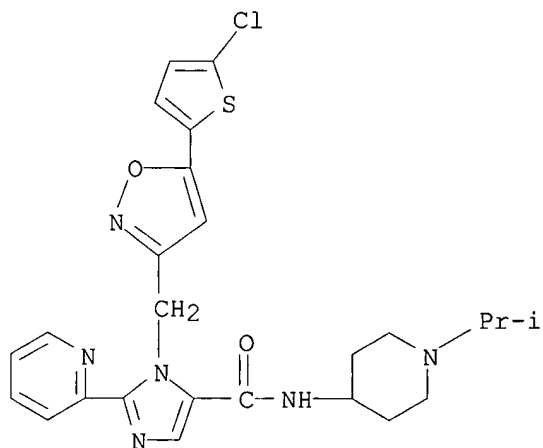
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-(1-methylethyl)-N-[1-(1-methylethyl)-4-piperidiny]- (9CI) (CA INDEX NAME)

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RN 701292-81-1 CAPLUS

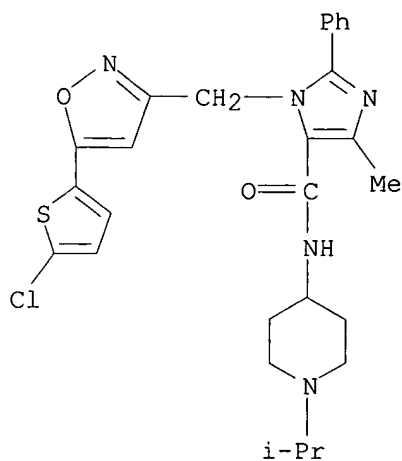
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidinyl]-2-(2-pyridinyl)-(9CI) (CA INDEX NAME)



RN 701292-82-2 CAPLUS

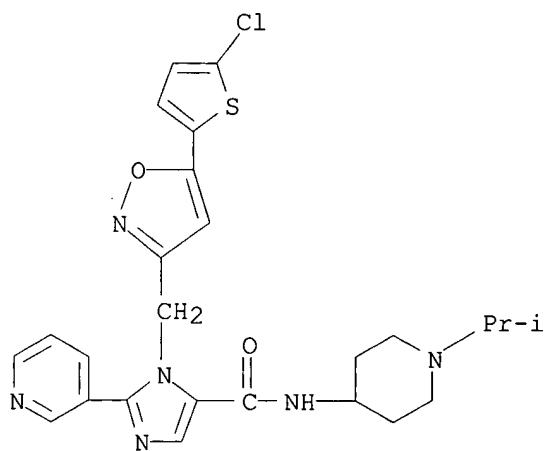
CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]-2-phenyl-(9CI) (CA INDEX NAME)

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RN 701292-86-6 CAPLUS

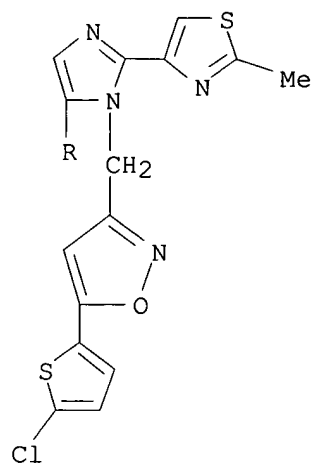
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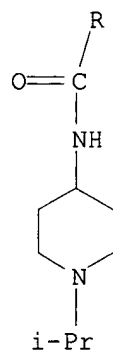
RN 701292-87-7 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidinyl]-2-(2-methyl-4-thiazolyl)- (9CI) (CA INDEX NAME)

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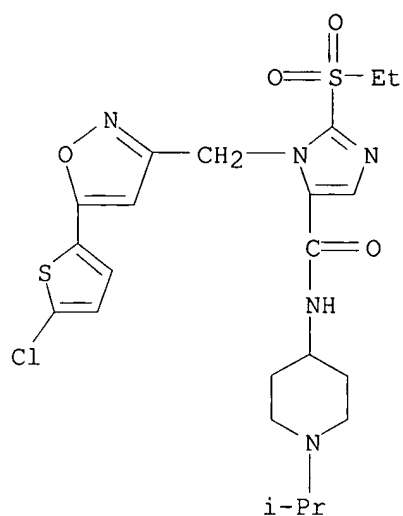


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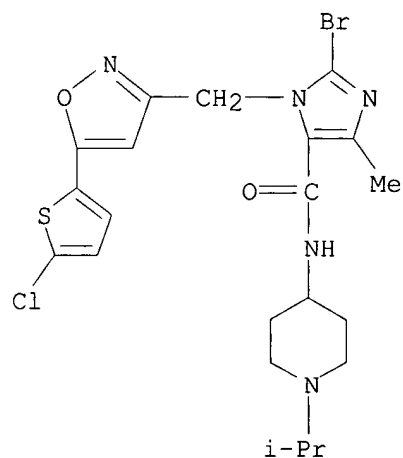
RN 701292-92-4 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-(ethylsulfonyl)-N-[1-(1-methylethyl)-4-piperidinyl]-(9CI) (CA INDEX NAME)



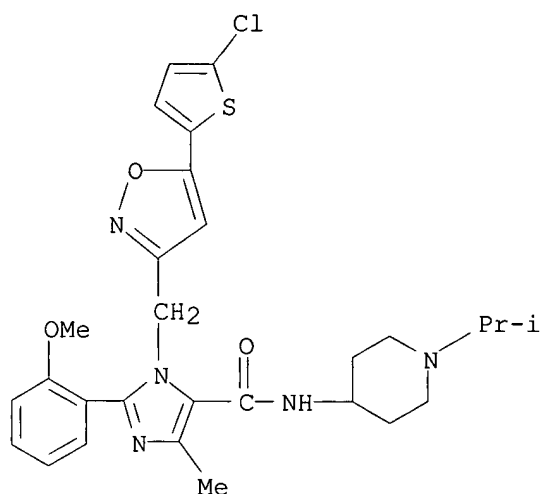
RN 701292-99-1 CAPLUS

CN 1H-Imidazole-5-carboxamide, 2-bromo-1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]- (9CI)
(CA INDEX NAME)



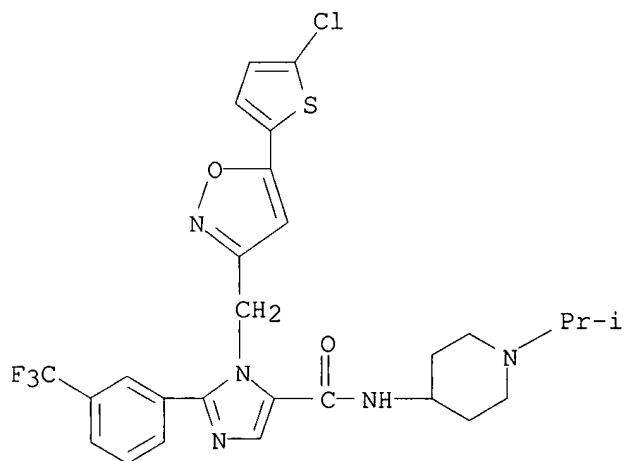
RN 701293-13-2 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-2-(2-methoxyphenyl)-4-methyl-N-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 701293-14-3 CAPLUS

CN 1H-Imidazole-5-carboxamide, 1-[[5-(5-chloro-2-thienyl)-3-isoxazolyl]methyl]-N-[1-(1-methylethyl)-4-piperidinyl]-2-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of imidazole derivs. of formula I [wherein: R1 is H, (un)substituted alkyl, monocyclic or bicyclic aryl, etc.; R2 is a bond or alkylene; R1 and R3 together with the atoms to which they are bonded form a 4-7-membered ring containing 1-4 heteroatoms; R1-N-R2-V form a 4-7-membered ring containing 1-4 heteroatoms; or R3 and R4 are independently selected from H, halogen, alkyl, Ph, NO₂, CN, or OH, etc.; R5 is monocyclic or bicyclic (hetero)aryl; Q is a bond, alkylene, SO₂, or NHC(O)NH, etc.; M is H, (hetero)aryl, cycloalkyl, C(O)NH₂, etc.; V is (hetero)aryl or a cyclic residue; G is a bond or -(CH₂)₁₋₆-NH-SO₂-NH-

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(CH₂)₁₋₆, etc.], useful as factor Xa inhibitors. The invented compds. exhibit a strong antithrombotic effect and are suitable, for example, for the therapy and prophylaxis of cardiovascular disorders like thromboembolic diseases or restenosis. Compds. I are reversible inhibitors of the blood clotting enzymes factor Xa (FXa) and/or factor VIIa (FVIIa), and can be applied in conditions in which an undesired activity of factor Xa and/or factor VIIa is present, or for the cure or prevention of which an inhibition of factor Xa and/or factor VIIa is intended. For instance, imidazole derivative II (inhibition constant of factor Xa is 0.065 μ M) was prepared via N-alkylation of Me 3H-imidazole-4-carboxylate by isoxazole derivative III, hydrolysis of the obtained imidazolecarboxylate derivative IV, and subsequent amidation by (1-isopropyl-piperidine-4-yl)amine hydrochloride (example 1).

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